



\* P < 0.001 vs. CaoV3

**Supplemental Figure 1.** Cell lines with the KRAS-variant (BG-1 and IGROV1) have significantly lower levels of *let-7b* compared to a non-variant cell line (CaoV3). Statistical analysis was done with a one way-Anova and Tukey's Multiple comparison test.

**A.** KRAS non-variant sequence

5' CCUGACCUCAGUGAUUCACCCACCUUGGCCUUAACCUG 3'

**B.** KRAS-variant sequence

5' CCUGACCUCAGUGAUGCACCCACCUUGGCCUUAACCUG 3'

ggacuggagugucacuacgugg 1-3 variant targeting siRNA

gaggacuggaguguucacuacggu 2-3 variant targeting siRNA

ggacuggaguguucacuacgugu 1-2 variant targeting siRNA

ugaggacuggaguguucacuacu 3-2 variant targeting siRNA

**Supplemental Figure 2.** Alignment of RNA oligos to the KRAS-variant sequence: (A) Non-variant sequence. (B) Variant siRNA oligos targeted to the KRAS-variant sequence. Underlined sequence depicts the *let-7* binding site. Red nucleotide represents targeted nucleotide (non-variant in (A)). siRNAs are shown starting with their 3' end.

**Supplemental Table 1: The KRAS-variant and overall survival in EOC patients with deleterious BRCA mutations (*n* = 79)**

Variable	HR	95% CI	p value
<b>KRAS status</b>	0.75	0.21 – 2.72	0.66
<b>Age</b>	1.01	0.98 – 1.05	0.45
<b>Stage</b>			0.0005
Stage III vs. Stage I and II	14.79	1.87 – 117.29	0.01
Stage IV vs. Stage I and II	69.98	7.00 – 699.87	0.0003
<b>Grade</b>			
Grade 2 and 3 vs. Grade 1	4.32	1.29 – 14.46	0.02
<b>Center (non Yale vs. Yale)</b>	0.66	0.23 – 1.87	0.43

HR: hazards ratio obtained from Cox proportional Hazards multivariate analysis

CI: confidence interval

Studies Included: Yale New Haven Hospital, City of Hope

**Supplemental Table 2. The KRAS-variant predicts suboptimal debulking after neoadjuvant chemotherapy (*n* = 116)**

KRAS-variant Genotype	Univariate			Multivariate <sup>3</sup>		
	OR <sup>1</sup>	95% CI <sup>2</sup>	p	OR	95% CI	p
<b>All</b>						
<b>Wild-type (<i>n</i>=90)</b>	1.00			1.00		
<b>Variant (<i>n</i>=26)</b>	5.27	1.10 – 25.30	0.0377	9.36	1.34 – 65.22	0.0240

1. OR: odds ratio obtained from logistic regression

2. CI: confidence interval

3. Multivariate: adjusted for age, stage, grade, histology, type of chemotherapy regimen, and numbers of cycles received prior to surgery.

**Supplemental Table 3. Clinicopathologic parameters for overall survival analysis**

Variable name	Non-variant (n=351)	KRAS-variant (n=103)	p value
Age (standard deviation)	60.44 (11.89)	58.77 (11.59)	0.2115
Stage			0.8627
I	52 (14.81)	15 (14.56)	
II	22 (6.27)	6 (5.83)	
III	193 (54.99)	52 (50.49)	
IV	80 (22.79)	29 (28.16)	
Unknown	4 (1.14)	1 (0.97)	
Grade			0.0507
Well differentiated	31 (8.83)	14 (13.59)	
Moderately differentiated	60 (17.09)	8 (7.77)	
Poorly differentiated	228 (64.96)	74 (71.84)	
Unknown	32 (9.12)	7 (6.80)	
Histology			0.1887
Serous	203 (57.83)	52 (50.49)	
Endometrioid	37 (10.54)	16 (15.53)	
Undifferentiated	7 (1.99)	0 (0.00)	
Clear Cell	21 (5.98)	10 (9.71)	
Mucinous	19 (5.41)	2 (1.94)	
Carcinosarcoma	13 (3.70)	7 (6.80)	
Mixed	19 (5.41)	6 (5.83)	
Unknown	32 (9.12)	10 (9.71)	
Center			0.2670
Yale New Haven Hospital	160 (45.48)	38 (36.89)	
Italy #1	146 (41.60)	51 (49.51)	
Italy #2	45 (12.82)	14 (13.59)	
Follow up Time (std deviation)	40.40 (33.57)	36.02 (29.40)	0.2324

**Supplemental Table 4. Clinicopathologic parameters for *BRCA* mutant EOC patients**

Variable name	Non-variant (n=69)	KRAS-variant (n=10)	P value
Age	52.77 (10.20)	52.60 (12.47)	0.9623
Stage			0.1771
I	5 (7.25)	2 (20.00)	
II	8 (11.59)	2 (20.00)	
III	51 (73.91)	5 (50.00)	
IV	5 (7.25)	1 (10.00)	
Grade			0.5275
Well differentiated	2 (2.90)	1 (10.00)	
Moderately differentiated	13 (18.84)	1 (10.00)	
Poorly differentiated	49 (71.01)	8 (80.00)	
Unknown	5 (7.25)	0 (0.00)	
Histology *			0.9913
Serous	8 (11.59)	1 (10.00)	
Endometrioid	2 (2.90)	0 (0.00)	
Undifferentiated	1 (1.45)	0 (0.00)	
Clear Cell	1 (1.45)	0 (0.00)	
Mucinous	1 (1.45)	0 (0.00)	
Carcinosarcoma	1 (1.45)	0 (0.00)	
Mixed	1 (1.45)	0 (0.00)	
Unknown	54 (78.26)	9 (90.00)	
BRCA status			0.7206
BRCA 1	51 (73.91)	7 (70.00)	
BRCA 2	18 (26.09)	3 (30.00)	
Center			0.6808
Yale New Haven Hospital	16 (23.19)	1 (10.00)	
City of Hope	53 (76.81)	9 (90.00)	

\* Histology information was not available for City of Hope patients

**Supplemental Table 5. Clinicopathologic parameters of patients receiving neoadjuvant chemotherapy**

Variable name	Non-variant (n=97)	KRAS-variant (n=28)	p value
Age (standard deviation)	64.30 (12.12)	62.57 (13.33)	0.5170
Ethnicity			0.5889
Caucasian	90 (92.78)	27 (96.43)	
Other or unknown	7 (7.21)	1 (3.57)	
Stage			0.0175
II	1 (1.03)	0 (0.00)	
III	41 (42.27)	4 (14.29)	
IV	51 (52.58)	23 (82.14)	
Unknown	4 (4.12)	1 (3.57)	
Grade			0.1308
Well differentiated	2 (2.06)	0 (0.00)	
Moderately differentiated	13 (13.40)	0 (0.00)	
Poorly differentiated	68 (70.10)	25 (89.29)	
Unknown	14 (14.43)	3 (10.71)	
Histology			0.8176
Serous	73 (75.26)	19 (67.86)	
Endometrioid	2 (2.06)	0 (0.00)	
Undifferentiated	2 (2.06)	0 (0.00)	
Clear Cell	4 (4.12)	2 (7.14)	
Mucinous	1 (1.03)	0 (0.00)	
Carcinosarcoma	1 (1.03)	1 (3.57)	
Mixed	6 (6.19)	3 (10.71)	
Unknown	8 (8.25)	3 (10.71)	
Neoadjuvant Chemotherapy			0.2765
Carboplatin/ Paclitaxel	85 (87.63)	21 (75.00)	
Carboplatin/ Taxotere	1 (1.03)	1 (3.57)	
Carboplatin/ Cyclophosphamide	7 (7.22)	5 (17.86)	
Other	4 (4.12)	1 (3.57)	
Neoadjuvant cycles completed:			0.3502
2	2 (2.06)	0 (0.00)	
3	4 (4.12)	2 (7.14)	
4	18 (18.56)	2 (7.14)	
5	4 (4.12)	4 (14.29)	
6	64 (65.98)	20 (71.43)	
7	3 (3.09)	0 (0.00)	
9	1 (1.03)	0 (0.00)	
Unknown	1 (1.03)	0 (0.00)	
Follow up time	30.53 (25.45)	36.54 (36.06)	0.3229

**Supplemental Table 6. Clinicopathologic parameters for platinum resistance analysis**

Variable name	Non-variant (n=225)	KRAS-variant (n=66)	p value
Age	58.66 (11.70)	56.11 (10.16)	0.1129
Stage:			0.9652
I	41 (18.22)	10 (15.15)	
II	19 (8.44)	6 (9.09)	
III	142 (63.11)	43 (65.15)	
IV	22 (9.78)	7 (10.61)	
Unknown	1 (0.44)	0 (0.00)	
Grade:			0.0728
Well differentiated	18 (8.00)	12 (18.18)	
Moderately differentiated	42 (18.67)	7 (10.61)	
Poorly differentiated	150 (66.67)	44 (66.67)	
Unknown	15 (6.67)	3 (4.55)	
Histology:			0.6319
Serous	114 (50.67)	31 (46.97)	
Endometrioid	33 (14.67)	10 (15.15)	
Undifferentiated	27 (12.00)	7 (10.61)	
Clear Cell	14 (6.22)	8 (12.12)	
Other	37 (16.44)	10 (15.15)	
Platinum response:			0.0340
Sensitive	208 (92.44)	55 (83.33)	
Resistant	17 (7.56)	11 (16.67)	
Cytoreductive surgery:			0.4808
Optimal cytoreduction (<1cm residual disease)	129 (57.33)	38 (57.58)	
Suboptimal cytoreduction (>1cm residual disease)	89 (39.56)	28 (42.42)	
Unknown	7 (3.11)	0 (0.00)	
Center			0.2808
Yale New Haven Hospital	55 (24.44)	10 (15.15)	
Italy #1	137 (60.89)	46 (69.70)	
Italy #2	33 (14.67)	10 (15.15)	
Follow up Time	39.08 (24.97)	36.47 (26.81)	0.4635